



A Case Report of Reversal of Cancer Cachexia and Literature Review

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Abstract

Cancer cachexia, as a special malnutrition, has poor efficacy with nutritional support alone. Patients with cachexia are likely to experience reduced quality of life and survival. Timely and effective intervention can reverse cachexia and improve the clinical outcome of patients. This patient was diagnosed as esophageal cancer, accompanied by cachexia, esophageal fistula, anemia and hypoproteinemia. After combination therapy, including nutritional support, metabolic regulation, anti-tumor treatment and symptomatic treatment, the patient's symptoms were significantly relieved, and cachexia was reversed. The quality of life was improved tumor was significantly reduced.

Introduction

The clinical incidence of cancer cachexia is relatively high. Epidemiological study of more than 40,000 tumor patients in China shows that the incidence of cachexia is as high as 37% [1], which is higher in digestive system tumors than in other tumors. In another systematic review, the prevalence of 5-year cachexia at risk is estimated about 30% in all cancer patients in the USA and EU [2]. It is well known that cachexia is to be associated with decreased quality of life, reduced tolerance to anti-tumor therapy and reduced survival. Hence, there is a large unmet clinical need for therapy of cachexia. Most patients diagnosed esophageal cancer are already in locally advanced stage or have distant metastasis, and suffer from cachexia and various complications. Without timely and effective intervention, the quality of life and prognosis of those patients will be seriously affected [3]. As a special malnutrition state, cancer cachexia is characterized by persistent skeletal muscle loss, with or without loss of adipose tissue, often accompanied by anorexia, fatigue, anemia, hypoproteinemia, electrolyte imbalance, infection, etc. Meanwhile, it is accompanied by gradual damage to the functions of the heart, lungs and other organs. The pathophysiology is characterized by abnormal metabolism and negative balance of protein and energy caused by reduced intake. It is a multi-factor syndrome [4].

Cancer cachexia has its own characteristics and pathophysiological mechanism. It cannot be fully reversed by conventional nutritional support. However, cancer cachexia does not refer to the end-stage of the disease, but can occur in any stage of malignant tumor, including newly diagnosed, postoperative and end-stage patients. Timely and effective intervention can partially reverse the disease, and then improve the clinical outcome of such patients.

Case Presentation

A 54-year-old man, went to the hospital because of "choking on food for more than 2 months" in June 2022. Contrast-enhanced CT of chest and abdomen showed significant thickening of the esophageal wall in the middle and lower segments, suggesting esophageal cancer. Multiple enlarged lymph nodes were found in the right cervical root, mediastinum, right hilum, gastric cardia. Esophagography showed the middle and lower esophagus wall was stiff and irregular filling defect. Besides, the mucosa was destroyed, interrupted and disappeared. The length of the lesion was about 16 cm, and local mediastinal fistula was possible. Gastroscopy showed an irregular raised neoplasm 25 cm away from the incisor teeth, full of lumen, narrow lumen, the endoscopic body could not pass through, surface erosion and necrosis, easy to bleed when touched.

Gastroscopic pathology: Well-differentiated squamous cell carcinoma. Immunohistochemistry (IHC22-10671): EGFR (2+), p53 (+80%), Ki-67 (+60%).

Laboratory examination: Hb 89 g/L, serum albumin 24.9 g/L, serum prealbumin 83 mg/L,

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Figure 1: Changes in body composition of patient.

SCC 4 ng/ml, CRP 112.6 mg/L, IL-6 81.11 pg/ml. He Had a history of smoking for more than 20 years, 20 cigarettes/day, and a history of drinking for more than 20 years, 0.25 kg/day. He denied history of chronic disease or family history of cancer. He came to our department for medical treatment on June 21st, 2022. At admission, he had obvious obstruction of feeding semifluid. Food intake decreased by about 1/3, and weight lost 5 kg in the past 2 months (weight loss rate was 9%).

Physical examination: ECOG:1, KPS: 70, Numeric Rating Scales (NRS, pain score): 2, Weight: 48.9 kg, Hight: 178 cm, Body Mass Index (BMI): 15.43, Patient-Generated Subjective Global Assessment (PG-SGA): C grade (9 points). He had an anxious, emaciated and anemic appearance, and no other positive signs were examined.

Admission diagnosis: Middle and lower esophageal well-differentiated squamous cell carcinoma with multiple lymph node metastases (cT3N3M0, stage IV), cancer cachexia (cachexia phase), esophageal mediastinal fistula? Cancer pain, hypoproteinemia, moderate anemia, mild anxiety.

This patient had multiple metastases of esophageal cancer, the presence of cancer cachexia, the possibility of esophageal mediastinal fistula, and the presence of anxiety, cancerous pain, hypoproteinemia, anemia. In view of the poor general condition of the patient at admission, anti-tumor therapy was not tolerated, and the efficacy of nutritional support alone wan not good effective. Thus, a "comprehensive treatment strategy" was adopted for this patient, including: 1) nutritional support: Naso-enteral nutrition tube was

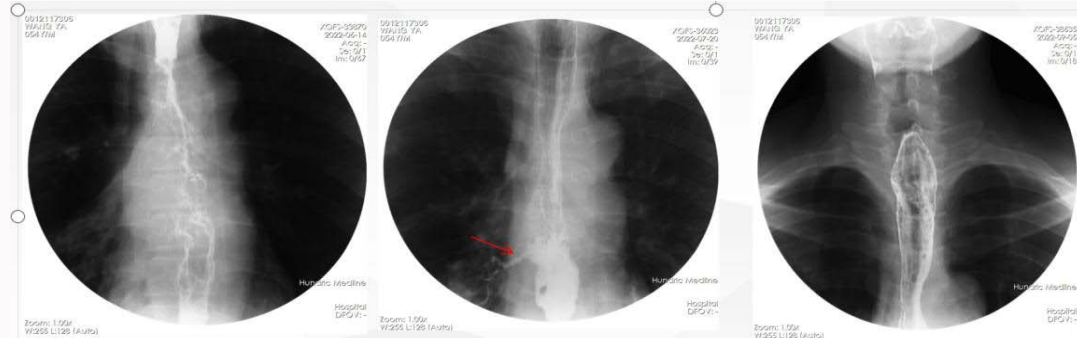
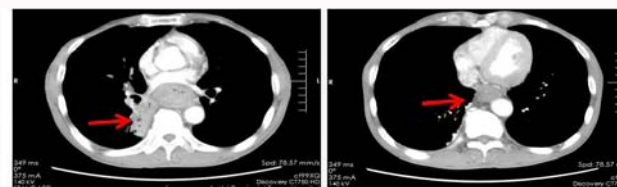


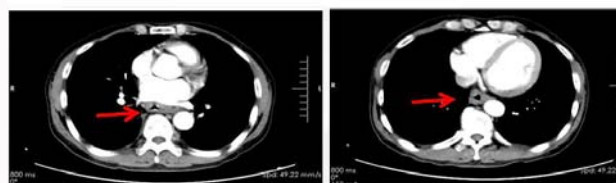
Figure 2: Esophagography, baseline, after 2 cycles of treatment, after 3 cycles of treatment.

inserted, and enteral (tumor specific enteral nutrition preparation + whey protein + homatropine methyl bromide) combined with partial parenteral nutrition support was performed. Calculation amount: 30 Kcal/kg. d, protein about 2 g/kg. d (gradually meet the demand in 3 days), carbohydrate and fat accounted for about 50% of the non-protein caloric calories; 2) Metabolic regulation treatment: The patient was treated with branched chain amino acids, nicotinamide glucose, insulin and megestrol; 3) Symptomatic treatment: Alleviated local edema of esophagus and relieved pain; 4) Psychological support: Communicated the cancer condition, the necessity of placing naso-intestinal nutrition tube and possible anti-tumor treatment plan to relieve anxiety and encouraged patients to actively get out of bed; 5) Anti-tumor etiology treatment: After the patient's symptoms improved and the target nutritional requirements basically met, the patient was treated with "carrelizumab 200 mg + albumin binding paclitaxel 0.2 d1, 0.1 d5 + cisplatin 30 mg D1-4" on June 24th, 2022, which was tolerated well. However, the patient had poor tolerance to the nasoenteric nutrition tube, which was removed by himself after discharge and ate orally.

On July 15th, 2022, the patient went to the hospital again, and his weight did not change significantly. PG-SGA score: Grade B (7 points). After admission, the angiogram showed that the esophageal lesions was better than before, and the esophageal mediastinal fistula was obvious. The gastroscopie showed that the mucosa was stiff 20 cm to 38 cm from the incisor teeth, a new protuberant creature could be seen on the periesophageal wall 30 cm to 37 cm, and a fistula with a diameter of about 4 mm could be seen at 35 cm. The naso-intestinal nutrition tube was placed again, and "comprehensive treatment" was given. The original scheme was treated for one cycle on July 17th, 2022. After discharge, the patient received total enteral nutrition treatment (1400 ml/d). During this period, diarrhea occurred, about 5 to 7 times a day. There was no abdominal pain and mucus bloody stool. On August 7th, 2022, he was admitted to the hospital due to "cough, expectoration with chest tightness and asthma after activities", and his body weight dropped by 4.4 kg over two weeks (the weight loss rate was about 9%). **Physical examination:** Emaciated and anemic appearance, naso-intestinal tube in position, thick breath sound of both lungs, audible moist rales, heart rate 102 times/min, regular rhythm, others were negative. On August 8th, 2022, chest and abdomen CT showed that the middle and lower esophageal wall was thickened, and the esophageal wall was significantly thinner than that in the front. The consolidation area of the adjacent right posterior mediastinum was narrowed. There were multiple enlarged lymph nodes near the trachea, in the mediastinum, and at the right pulmonary hilum, and some of them were smaller than that in the front; Multiple

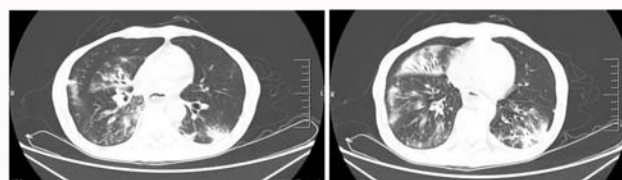


baseline: June 13, 2022

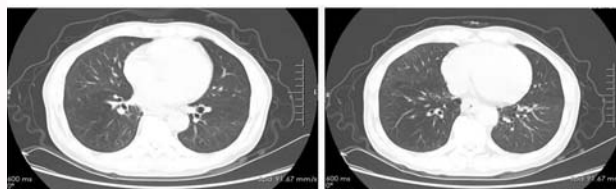


After 4 cycles: October 26, 2022

Figure 3: Contrast of patients with enhanced abdominal CT, PR at baseline and after 4 cycles of treatment.



Chest CT, after 2 cycles: August 18, 2022



Chest CT, after 4 cycles: October 26, 2022

Figure 4: Chest CT, lung infection after 2 cycles and after 4 cycles antitumor therapy.

inflammation of both lungs with bronchiectasis. PG-SGA score at admission was C (11 points), W: 44.5 kg, H: 178 cm, BMI: 14.04. Hb: 103 g/L, blood albumin: 32.6 g/L, prealbumin: 150 mg/L, SCC1: 4 ng/ml, CRP: 51.4 mg/L, PCT: 0.3 ng/ml. Sputum culture showed *Serratia marcescens*. The patient was given anti-infection, enteral nutrition (1400 ml/d, pay attention to temperature, speed and gradient),

anti-diarrhea, metabolic regulation, anti-anxiety, and symptomatic treatment of sleep adjustment. The patient's symptoms improved significantly. On August 13th, 2022, the patient was discharged after one cycle of anti-cancer treatment with the original protocol. On August 25th, 2022, the patient's naso-intestinal tube fell off outside the hospital and he did not go to the hospital. He ate by mouth without obvious cough, choking, pain and discomfort. On September 4th, 2022, his body weight increased from 44.5 kg to 54.3 kg, and skeletal muscle mass also increased significantly (Figure 1). Imaging showed that esophageal lesions were improved and esophagotracheal fistula was not obvious (Figure 2). On September 7th, 2022 and September 30th, 2022, the patients were treated with the original regimen for 2 cycles. Nutrition evaluation on October 25th, 2022: PG-SGA: Grade B (2 points), weight 60.1 kg, soft food taken orally to meet the nutritional requirements, anemia improved, albumin and prealbumin gradually returned to normal and maintained. The inflammatory indexes CPR, IL-6 and N/L gradually decreased from high to normal. On October 26th, 2022, chest and abdomen CT: The volume of esophageal lesions decreased, and most of the multiple lymph nodes were smaller than before, and lung infections also improved significantly; Evaluate PR (Figure 3, 4). He continued the original scheme on October 26th and November 17th, 2022. Now, he has a good quality of life tolerance to anti-tumor.

Discussion

Cancer cachexia is a kind of malnutrition and metabolic disorder characterized by "calorie-protein deficiency malnutrition". It originates from the insufficient intake and absorption of calories and nutrients in the patient's body, as well as the complex nutrient metabolic disorder and consumption caused by the stress state of the body and the production of various pro-decomposition cytokines by the tumor tissue. Under the joint action of the body and the tumor, the negative balance of protein and energy is eventually caused, and the body presents a state of cachexia [5,6]. Most patients are accompanied by hypoproteinemia, anemia, infection, gastrointestinal dysfunction and so on. Muscle loss caused by progressive skeletal muscle loss is the main cause of its clinical symptoms and poor prognosis. Conventional nutritional support and drug treatment are difficult to improve the nutritional metabolism disorder of patients with cancer cachexia, so the effect is poor and the progress of anti-cachexia is slow [7].

The key to improve and reverse the cachexia is to attack the tumor load, effectively reduce the metabolic activity of tumor tissue, and control the inflammatory state of the body. However, patients with cachexia usually cannot tolerate conventional anti-tumor drug treatment. So, treatment needs to take into account a variety of issues. Clinically, "comprehensive treatment" strategies are usually used to reverse cancer cachexia, including antitumor therapy, nutritional support, metabolic regulation therapy, repair and maintenance of gastrointestinal function, palliative therapy, psychological therapy and exercise. Our team includes medical staff and dietitians from the department of oncology and clinical nutrition and metabolism therapy. The "comprehensive treatment" strategies are used to reverse cachexia. The clinical effect was satisfactory, and a new treatment plan was explored for the treatment of cancer cachexia. When this patient was admitted to the hospital, his general condition was poor, and there were many complications. He was given active nutritional support (mainly in the intestine, maximize the use of intestinal function, and maintain the intestinal barrier function),

metabolic regulation treatment (combined use of multiple metabolic regulators), symptomatic reduction and psychological support. After the patient's symptoms improved, he was given anti-tumor treatment for etiology. During this period, the patient suffered from diarrhea due to poor method of parenteral nutrition outside the hospital and cachexia was caused again, which was reversed after active "comprehensive treatment". At present, the nutritional status of the patient is good, and the fistula is basically healed. There is no cough and infection through oral eating. The improvement of nutritional status is helpful to the healing of the fistula. In oncology, esophageal lesions were significantly improved and lymph nodes were shrunk. PR was evaluated. The tumor index SCC decreased to normal and maintained. Body weight increased 11.2 kg and muscle mass increased 4.4 kg from baseline. Anemia index improved, albumin and prealbumin significantly improved to normal, and inflammation index improved. The general condition and nutritional status were significantly improved, and the tolerance of anti-tumor treatment was good. At present, he continues the original anti-tumor treatment. The objective of improving the quality of life and prolonging the survival period of patients is achieved.

Conclusion

The high incidence of cancer cachexia is one of the main causes of death. Most patients have poor physical strength, and conventional nutritional support is difficult to reverse. Most patients cannot tolerate conventional anti-tumor treatment. It is important to accurately understand the mechanism of energy nutrient metabolism disorder and make correct nutritional diagnosis. Effective anti-tumor treatment provides basic guarantee for the improvement of abnormal metabolic status, and good nutritional status is the premise to ensure the smooth progress of anti-tumor. Metabolic regulation treatment can reverse the nutritional status of tumor patients, reduce chemotherapy induced toxicity, and improve chemotherapy tolerance and efficacy. The maintenance of gastrointestinal function provides an input way for nutritional support and reduces the risk of infection. Psychological regulation and physical activity can improve the patient's mood and promote the recovery of gastrointestinal function. Reducing consumption and symptomatic treatment can improve the patient's quality of life.

In conclusion, primary disease treatment is the premise, and nutritional support is the basis. Metabolic regulation is the key, and inhibition of inflammation is fundamental. A variety of treatment methods should be taken into account to reverse cancer cachexia and improve the quality of life and survival of patients.

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